Exhibit A
Part 1

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327**
THIS DOCUMENT RELATES TO	**JOSEPH R. GOODWIN**
WAVE 5 CASES	**U.S. DISTRICT JUDGE**

RULE 26 EXPERT REPORT OF BRUCE ROSENZWEIG, M.D.

I. QUALIFICATIONS.

I am currently an Assistant Professor of Obstetrics and Gynecology at Rush University Medical Center in Chicago, Illinois. I received my MD degree in 1984 from the University of Michigan in Ann Arbor, Michigan. Following graduation from medical school, I completed an Obstetrics and Gynecology Residency at Michael Reese Hospital in Chicago. In 1988, I attended a one year pelvic surgery fellowship at State University of New York in Syracuse, New York. Following that fellowship, I attended a two year Urogynecology and Urodynamics fellowship at UCLA Harbor General Hospital in Torrance, California. After graduating from the Urogynecology fellowship, I became a faculty member at the University of Illinois in Chicago. I started a Urogynecology program at the University of Illinois and also was the residency program director. In 1998, I went into private practice, and subsequently established a private practice at Rush University Medical Center. I have also worked at John H. Stroger Hospital here in Chicago from May 2003 until November 2010 and Weiss Memorial Hospital as Associate Chair of Gynecology from February 2011 until

July 2012. I have published numerous articles and given numerous lectures on the topics of pelvic organ prolapse, urinary incontinence and repair of pelvic organ prolapse.

Throughout my career, I have performed over a thousand pelvic floor surgical procedures, including abdominal sacrocolpopexy, uterosacral suspensions, sacrospinous ligament fixations, native tissue repairs, biological graft repairs and synthetic mesh repairs. I have also used numerous synthetic pelvic mesh products, including Ethicon's TVT, TVTbturator, and Prolift. In addition, I have performed over 300 surgeries dealing with complications related to synthetic mesh, including the removal of numerous TVT devices. I have also treated approximately 800 additional patients with mesh non-surgically. I was invited by Ethicon and attended both its Gynecare Prolift Training Seminar and TVT Obturator Seminar in Belgium. In addition, I was invited and attended a Bard Avaulta training seminar in the past.

A copy of my CV and Fee Schedule is attached as Exhibit "A" and a copy of my testimony for the last four years is attached as Exhibit "B". The documents I relied on for this report are contained in Exhibit "C" as well as those documents cited throughout this Report.

II. SUMMARY OF OPINIONS.

In formulating my opinions and preparing this report, I reviewed scientific literature, corporate documents from Ethicon, sample products and depositions of Ethicon employees and witnesses. The corporate documents, sample products and depositions were supplied to me by counsel. A list of Ethicon corporate documents and depositions reviewed for this report is attached hereto as Exhibit "C"; other materials reviewed are listed at the end of this report. All opinions I have are to a reasonable degree of medical and scientific certainty. I understand discovery is still ongoing in this case, and I reserve my right to amend my opinions if further information is provided in any form including, but not limited to corporate documents,

depositions and the expert reports of both Plaintiff and Defense experts. My opinions in this Report relate only to the Ethicon Design Consolidation case pending in West Virginia.

In general, my expert opinions can be summarized as follows[1]:

A. Ethicon's old construction mesh (Prolene), used in the TVT, is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence because the pores are too small, it is heavy weight mesh, it degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, fraying, particle loss, biofilm formation and infections, has sharp edges, ropes, curls and deforms, and the pores collapse with tension;

B. Ethicon knew that the old construction mechanically cut mesh (Prolene) was not appropriate for use in its TVT device but has failed to modify/change the mechanically cut mesh to a larger pore, lighter weight mesh that would not deform, fray, lose particles, rope, curl, degrade, cause excessive foreign body reactions, and cause excessive shrinkage/contraction. According to Ethicon's internal documents, Ethicon was unwilling to change the mesh because of its economic interest in maintaining its competitive advantage in the MUS market and, therefore, Ethicon put profits before patient safety;

C. The Laser Cut Mesh Is also inappropriate for Use as a permanent implant because it is too stiff and rigid and causes pain and erosions and urinary dysfunction as a result

D. Ethicon's TVT's design is flawed because it cannot adequately describe, inform or explain to physicians how to properly "tension" the TVT and the mesh shrinks, contracts, ropes and curls making it difficult or impossible to tension in a safe manner for patients;

E. Ethicon's Prolene mesh in the TVT is not suitable for permanent implant because the Material Safety Data Sheets ("MSDS") for polypropylene resin used to manufacture polypropylene states that polypropylene is incompatible with strong oxidizers such as peroxides which are readily found in the vagina;

F. Ethicon's Prolene mesh is also not suitable for permanent implant because the toxicity testing of the polypropylene mesh revealed that it was cytotoxic which can cause cell death and complications;

G. Ethicon's warnings and disclosures of adverse events in its TVT Instructions for

[1] This is not intended to be an exhaustive recitation of my opinions in this case. The full scope of my opinions are described in further detail in this report.

Use ("IFU") have been inadequate based on the adverse reactions and risks associated with the TVT that have been known to Ethicon from the time the TVT was first sold and marketed, and Ethicon did not disclose information to physicians in its IFUs regarding characteristics of the old construction mesh (Prolene) that makes it unsuitable for its intended application as a permanent prosthetic implant for stress urinary incontinence, including that it is small pore, heavy weight mesh, it degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, fraying, particle loss, roping and curling of the mesh, that it deforms and the pores collapse with tension, that it is difficult or impossible to tension; that it tested positive for cytotoxicity and that the MSDS states that it is incompatible with strong oxidizers such as peroxides.

H. The design of the TVT device is flawed because it is not designed for special patient populations nor does the IFU or marketing documents inform physicians that certain patients will have poorer outcomes and higher risks.

I. Ethicon failed to reveal material facts about complication and conflict of interests regarding key studies and in key marketing documents.

J. The benefits of the TVT are outweighed by the severe, debilitating and life changing complications associated with the TVT and there were safer alternative options available.

K. It has been known since the launch of the TVT that the mesh can be difficult to remove, is susceptible to degradation, can rope, curl, deform, fray, and lose particles, and is a heavy weight mesh. However, Ethicon did not account for this facts in its dFMEA at the time of launch, and has failed to complete a proper risk analysis of these hazards

III. BACKGROUND AND TREATMENT OPTIONS FOR STRESS URINARY INCONTINENCE.

A. Stress Urinary Incontinence ("SUI")

Approximately one of three women over the age of 45 years old has some form of urinary incontinence. The majority of those women do not seek medical advice or treatment for a variety of reasons.

In a continent individual, increased abdominal pressure is evenly distributed over the bladder, bladder neck, and urethra. The urethral sphincter is thus able to withstand this pressure and maintain continence. In a person with pure stress urinary incontinence (SUI),

either the urethra is hypermobile or the sphincter is intrinsically deficient. In urethral hypermobility, the urethrovesical junction (UVJ) is displaced extra-abdominally, and the increased intra-abdominal pressure is unevenly distributed such that the sphincter can no longer withstand the pressure and urine leaks. With intrinsic sphincter deficiency (ISD), the UVJ is not hypermobile; however, the maximal urethral closing pressure, the Valsalva leak-point pressure, or both are too low to withstand the increase in intra-abdominal pressure and, thus, urine leaks past the sphincter.

SUI is the involuntary leakage of urine during moments of physical activity that increases abdominal pressure, such as coughing, sneezing, laughing, or exercise, in the absence of a bladder contraction. It has been estimated that 14% of women have SUI. SUI is a common type of urinary incontinence in women. Urodynamic proven SUI is found in approximately 50% of women presenting for evaluation of urinary incontinence. Symptomatic women with SUI have social or hygienic consequence from their urine loss. SUI can happen when pelvic tissues and muscles, which support the bladder and urethra, become weak and allow the bladder "neck" (where the bladder and urethra intersect) to descend during bursts of physical activity (urethral hypermobility). This descent can prevent the urethra from working properly to control the flow of urine. SUI can also occur when the sphincter muscle that controls the urethra weakens (intrinsic sphincter deficiency). The weakened sphincter muscle is not able to stop the flow of urine under normal circumstances, and when there is an increase in abdominal pressure. Weakness may occur from pregnancy, childbirth, aging, or prior pelvic surgery. It has been estimated that a majority of incontinent women have a combination of urethral hypermobility and ISD. Other risk factors for SUI include chronic coughing or straining, constipation, obesity and smoking. Finally occult or latent SUI is defined as a positive stress test, loss of urine with increased intra-abdominal pressure and between 350-

450cc volume in the bladder, after the repositioning of pelvic organ prolapse (usually accomplished with a ring pessary carefully positioned as to avoid compression of the urethra) in an otherwise clinically continent patient.

B. Nonsurgical Treatment of SUI.

There are numerous non-surgical treatments available to woman with SUI. First, Pelvic Floor Exercises: A type of exercise to strengthen the pelvic floor by contracting and relaxing the levator muscles that surround the opening of the urethra, vagina, and rectum. These exercises, commonly referred to as Kegel exercises, improve the pelvic floor muscles' strength and function. Kegel exercises can improve over-active bladders by increasing urethral resistance with can trigger the bladder to relax.

Second, Pessary: A removable device that is inserted into the vagina against the vaginal wall and urethra to support the bladder neck. This helps reposition the urethra to reduce SUI. These can be made of rubber, latex or silicon. Inserted into the vagina, a pessary rests against the back of the pubic bone and supports the bladder. Pessaries are available in various forms, including donut and cube shapes, and must be fitted by a healthcare provider. Some women who have stress incontinence use a pessary just during activities that are likely to cause urine leakage, such as jogging. Special incontinence pessaries have a 'knob', which fits under the urethra to elevate the midurethral to prevent urine loss.

Third, Transurethral Bulking Agents: Bulking agent injections are applied around the urethra that makes the space around the urethra thicker, thus helping to control urine leakage. The effects are usually not permanent.

Fourth, Behavioral Modification: This includes avoiding activities that trigger episodes of leaking. Lifestyle modification can improve stress incontinence symptoms and include quitting smoking, weight loss, and allergy treatment during seasonal allergies.

Fifth, Urinary seals: These are adhesive foam pads, which women place over the urethral opening. The pad creates a seal and prevents the leakage of urine, providing incontinence treatment. The pad is removed before urination and replaced with a new one afterward. The pad can be worn during exercise or physical activity, but not during sexual intercourse.

Sixth, Urethral insert: A thin, flexible tube that is solid rather than hollow (like a catheter) is placed into the urethra to block the leakage of urine. These small plugs are inserted into the urethra by women to prevent leakage, and are removed prior to urination. These inserts can be uncomfortable and may increase the risk of urinary tract infection.

Seventh, Bladder neck support device: This device is a flexible ring with two ridges. Once inserted into the vagina, the ridges press against the vaginal walls and support the urethra. By lifting the bladder neck, it provides better bladder control in women suffering from stress incontinence. The device needs to be sized to fit, and must be removed and cleaned after urination. Bladder neck support devices can be uncomfortable and may cause urinary tract infections.

C. Surgical Treatment of SUI.

1. <u>The Burch Colposuspension</u>.

Retropubic approaches for the treatment of stress urinary incontinence include the Burch retropubic urethropexy (both open and laparoscopic) and the Marshall-Marchetti-Krantz (MMK) procedure. The goal of both of these procedures is to suspend and stabilize the urethra so that the urethrovesical junction (UVJ) and proximal urethra are replaced intra-abdominally and to recreate a firm backstop for intra-abdominal pressure. This anatomic placement allows normal pressure transmission during periods of increased intra-abdominal pressure restoring continence in a previously incontinent, hypermobile UVJ.

The Burch procedure was described in 1961. Initially, Burch described attaching the paravaginal fascia to the arcus tendineus. However, this was later changed to Cooper's ligaments because these were felt to provide more secure fixation points, and less chance of infection as seen with the prior MMK procedure.

Patients with type III stress urinary incontinence (a fixed, nonfunctioning proximal urethra) are not ideal candidates for a Burch procedure as no hypermobility exists to correct. For the Burch procedure, a low Pfannestiel incision is made above the pubic bone in order to enter the space of Retzius (the anatomical space between the pubic bone and the bladder above the peritonium in order to suspend the bladder and/or to perform a paravaginal repair. The procedure involves placing permanent stitches adjacent to the neck of the bladder and either proximal or distal to the bladder neck stitches on each side and suturing them Cooper's ligament which is attached to the pubic bone. The paravaginal repair is very similar except that the stitches are attached to the arcus tendentious linea pelvis. The likelihood of success of the Burch and the paravaginal repair procedures is reported to be 80-90% in most cases. Success means total elimination of the incontinence and patient satisfaction score greater than 90%. Improved means significant reduction of urine loss and greater than 70% improvement of patient satisfaction scores. Additionally, these retropubic procedures can be accomplished by the laparoscopic route. With respect to the selection of synthetic absorbable suture versus non-absorbable suture, and braided versus monofilament, no prospective randomized blinded data exist to suggest superiority of one suture material over another. However, recognized risks are associated with bone anchors. Modifications in the technique can be used if co-existent central defect cystocele is present and obliteration of the cul-de-sac can be performed to prevent enterocele or posterior vaginal wall prolapse after Burch colposuspension.

Although the Burch procedure may take longer and require a very small hospitalization,

it is a much safer procedure than synthetic slings because life-altering long-term complications do not occur with Burch like they do with synthetic slings, including chronic debilitating pain, chronic sexual dysfunction and dyspareunia, erosions, multiple surgeries to remove mesh, emotional issues related to sexual dysfunction and many others as discussed throughout this report. Furthermore, if complications do occur following a Burch procedure, they are very rarely long-term and much easier to treat.

2. Pubovaginal sling procedures.

Pubovaginal slings have excelled overall success and durable cure. The procedure involves placing a band of autologous, allograft, xenograft or synthetic material directly under the bladder neck (ie, proximal urethra) or mid-urethra, which acts as a physical support to prevent bladder neck and urethral descent during physical activity. This is brought up through the rectus fascia. The sling also may augment the resting urethral closure pressure with increases in intra-abdominal pressure.

Historically, surgeons have used the fascia lata sling for recurrent SUI after a failed anti- incontinence operation. Furthermore, this operation is used extensively for the treatment of primary ISD. If the abdominal tissues are weak and attenuated or if the vaginal tissues are atrophied or in short supply, constructing a pubovaginal sling from the leg fascia lata can be performed. This procedure is more involved than the creation of the rectus fascial sling as it requires a second incision to harvest the fascia lata and healing in an area remote for the index procedure.

An alternative to a long rectus sling is construction of a short sling from a much smaller piece of abdominal fascia (rectus fascia suburethral sling). The surgical procedure is similar to that used for the rectus fascia pubovaginal sling, except that the harvested fascial tissue is much smaller and the operation time shorter. The advantage of this procedure is its simplicity. No

extensive dissection in the suprapubic area is necessary, and the postoperative result is similar to that of the full-length fascial strip sling.

An alternative to a long fascia lata sling is the use of a postage stamp–sized patch of fascia lata from the outer thigh (fascia lata suburethral sling). The surgical procedure is similar to that for the fascia lata pubovaginal sling, except the harvested fascia is much smaller. This operation does not require extensive dissection in the thigh area, and the postoperative result is similar to that of the full-length fascia lata strip sling. Postoperative convalescence is shorter than that of the fascia lata pubovaginal sling procedure.

The vaginal wall suburethral sling helps restore urethral resistance by increasing urethral compression and improving mucosal coaptation of the bladder neck. This operation is attractive because it is simple and easy to perform. Postoperative complications are minimal, and the recuperative period is short. Vaginal sling surgery is relatively contraindicated in elderly women with atrophic vaginitis. If recognized before surgery, the atrophied vaginal wall may be revitalized with the administration of vaginal estrogen cream or tablets for 3-6 months.

A clear contraindication to pubovaginal sling surgery is pure urge incontinence or mixed urinary incontinence (MUI) in which urge is the predominant component. An inherent risk of any sling procedure is de novo or worsening urge symptoms; thus, surgeons must identify and treat the presence of an urge component before surgery.

Conversely, poor detrusor function is a relative contraindication to pubovaginal sling surgery because the potential for urinary retention is increased. Women with absent or poor detrusor function in the presence of SUI are at a higher risk of experiencing prolonged postoperative urinary retention.

3. <u>Midurethral Synthetic Slings</u>.

Based on the "Integral theory of female incontinence," Prof. Ulmsten developed a

midurethral procedure to treat stress urinary incontinence. The first reports of this procedure appeared in 1996 as an intravaginal slingoplasty. The "tape'" was place through a small vaginal incision at the midurethra, brought through the urogenital diaphragm through the retropubic space and exited through small suprapubic incisions. The operation was theorized to correct incontinence by recreating the midurethral support of the pubourethral ligament and also by creating a midurethral hammock for support of the urethra during stress events. The procedure was described to have a success rate of 85-90% with an additional 5-10% significantly improved. The Gynecare TVT system was introduced in the US in November of 1998. Early studies showed that the risk of bladder perforation during the procedure occurred 5-10% of cases and vascular injury with without hematoma formation occurred in 2-5% of patients.

In an attempt to decrease the risk of bladder perforation and vascular injury, a "top-down" approach to trocar placement was promoted as the SPARC procedure, introduced in the US in 2001 by American Medical Systems (AMS). The next modification of the midurethral sling came in 2001 when Delorme described his results for the use of the obturator membrane and inner thigh for passage of the sling material. The proposed advantage was avoidance of the retropubic space, thus avoiding bladder perforation and retropubic vascular injury. The trocars were passed from the inner thigh through the obturator membrane from an "outside – in direction".

The next modification came from de Leval in 2003, with the "inside-out" trocar placement for the transobturator sling. This device is the focus of this report. The final modification came around 2006 with the release of the mini-slings, or single incision slings, which use support devices at the ends of shorter mesh lengths to accomplish fixation without the need for a secondary cutaneous exit point. The mini-slings could be placed in a retropubic

or "U" fashion or a hammock or "H" fashion.

The FDA concluded in 2011 that there was higher peri-operative blood loss, higher mesh exposure and greater need for surgical re-intervention in the TVT-Secur (mini-sling) patients.

IV. EXPERT OPINIONS

A. Ethicon's old construction mesh (Prolene), used in the TVT, is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence because the pores are too small, it is heavy weight mesh, it degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, fraying, particle loss, biofilm formation and infections, sharp edges, roping and curling of the mesh, it deforms, the pores collapse with tension, and it is too stiff and rigid.

Polypropylene mesh (Prolene), like that contained in the TVT, has many well-known characteristics that make it unsuitable for use as a product intended for permanent implantation in the human vaginal floor. These characteristics include the following: (1) degradation of the mesh; (2) chronic foreign body reaction; (3) infections and bio-films; (4) fraying, roping, curling and deformation of the mesh; (5) loss of pore size with tension; (6) fibrotic bridging leading to scar plate formation and mesh encapsulation; (7) shrinkage/contraction of the encapsulated mesh; and (8) the mesh is stiff and rigid.

As a result of these and other inadequacies with the mesh, and for the reasons set forth below, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT causes a multitude of injuries, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, nerve injury of the pelvic nerves, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. For the reasons discussed further in this report and its failure to

perform appropriate long term testing and studies, Ethicon realized very early on that it had problems with the mechanically cut mesh in the TVT products, through numerous complaints from physicians. As a result, they found a cheaper way to cut the mesh and prevent particle loss and fraying through laser cutting the mesh. As a result, for the reasons discussed throughout this report, Ethicon created a stiffer, more rigid piece of mesh that created another set of complications discussed in this report. As discussed more fully below, Ethicon failed to act like a reasonable manufacture and, as a result, Ethicon's TVT-O mesh (Prolene), whether mechanically cut or cut by a laser, is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women. Ethicon failed to adequately test the laser cut mesh, silently launched the mesh and misled physicians about the laser cut mesh.

1. The Prolene Mesh in TVT Degrades Over Time

As noted below, the mesh used in the TVT was originally designed in 1974 for use in the abdomen for treatment of hernias and it has not changed since then.[2] Ethicon describes this mesh as the "old, old" mesh: "The first generation (old, old) mesh is utilized currently in the TVT product…."[3] The current Material Specifications for TVT Mesh list it as: "Old Construction PROLENE* Mesh."[4] Dan Smith testified that even when the original hernia mesh was updated for use in the abdomen, Ethicon continued to use the "old, old" mesh for TVT and does to this day, as follows:

Q: So TVT kept the old when hernia changed to the new.
A: Also known as original, yes.
Q: The mesh that was used in the TVT-R is called sometimes by Ethicon in documents old construction or original mesh; correct?
A: Yes. Yes.[5]

In the late 90's Ethicon determined that, in the hernia applications, it was safer to move

[2] Smith Dep. (2/3/2014) 723:9-724:6.
[3] Smith Dep. (2/3/2014) 723:9-724:6.
[4] ETH.MESH.10633520 at 3522.
[5] Smith Dep. (2/3/2014) 723:9-724:6.

to a lighter weight, larger pore mesh. Ethicon made a similar determination for meshes to be used in the pelvic floor.[6] However, Ethicon never updated the "old, old" hernia mesh used in the TVT.[7] Notably, in my opinion this makes science and information regarding hernia meshes and other pelvic meshes of particular relevance when discussing the TVT mesh as Ethicon chose to move to large pore, light weight meshes in these areas, but not for TVT. Moreover, Ethicon relied on science and information regarding hernia meshes to claim the safety and efficacy of their pelvic mesh products to regulatory bodies.

The placement of permanent polypropylene mesh in the human vagina creates problems because of the chemical composition and structure of the mesh and the physiological conditions of the vagina and the surrounding tissues. There have been numerous studies over the last 30 years which have shown polypropylene to be chemically reactive and not inert, with flaking and fissuring demonstrated by scanning electron microscopy, which leads to degradation and release of toxic compounds into pelvic tissues. This process enhances the inflammatory and fibrotic reactions within the tissues in the pelvic floor, causing a multitude of problems.[8] There have been studies suggesting that oxidation of the mesh occurs because of the polypropylene and the conditions in which it is placed.[9] The oxidation causes the mesh to degrade, crack and break apart.[10] In a recent study, 100 pelvic mesh implants were compared and over 20% showed degradation to mesh fibers.[11] Because

[6] See, e.g., ETH.MESH.07455220 (discussing mesh shrinkage/contracture and stating: "Since this phenomenon occurs most frequently in small pore, heavy weight mesh, ETHICON has developed large pore, light weight meshes, i.e. GYNECARE GYNEMESH PS Nonabsorbable Prolene Soft Mesh….").
[7] Smith Dep. (2/3/14) 829:16-829:19.
[8] Coda A., *Hernia 2003*;7:29; Jongebloed,WL, "*Degradation of Polypropylene in the Human Eye: A SEM Study*," Doc. Ophthalmol., 1986 64(1:143-152); Skrypunch, O.W., "*Giant Papillary Conjunctivitis from an Exposed Prolene Suture*," Can. J Ophthalmology, 198621:(5: 189-192).
[9] Costello C., et al., "*Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants from a Single Patient*," Surgical Innovation , 2007, 143:168- 176).
[10] *Id.*
[11] Clavé A, Yahi H, Hammou JC, Montanari S, Gounon P, Clavé H, "*Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants,*" J Biomed Mater Res B Appl Biomater, 2007, Oct 83(1:44-9)

of the structural complexities of the vagina and the nature of the chemicals ordinarily found in the vagina and its surrounding tissues**,** there are several reasons why polypropylene presents unique problems when placed in the vagina. An Engineering Bulletin from Propex, entitled "*EB-405, The Durability of Polypropylene Geotextiles for Waste Containment Application,*" from 2011, states that, "[P]olypropylene is vulnerable to the following substances: highly oxidized substances such as (peroxide), certain chlorinated hydrocarbons (halogenated hydrocarbons), and certain aromatic hydrocarbons."[12] It is well known to physicians with expertise in the pelvic floor that vaginal and perivaginal tissues are ready sources for peroxide. The vaginal species lactobacillus produces hydrogen peroxide and lactic acid from collagen that is produced in the squamous cells of the vagina. Estrogen is the catalyst for the production of collagen from the vaginal cells. It is also well known that hydrogen peroxide produced by the lactobacillus species is important in controlling the vaginal micro-flora.

In fact, the vagina is a ready source of hydrogen peroxide production. In a manuscript from M. Strus, "*The In Vitro Effects of Hydrogen Peroxide on Vaginal Microbial Communities,*" the authors show the amount of hydrogen peroxide produced by the lactobacillus species.[13] "Hydrogen Peroxide reached concentrations of from 0.05 to 1.0 mm, which under intensive aeration increases even up to 1.8 mm."[14] These results confirmed the previous results of M. Strus in the publication, "*Hydrogen Peroxide Produced by Lactobacillus Species as a Regulatory Molecule for Vaginal Micro-flora*," Med Dosw Mikrobiol, 2004: 56(1:67-77).

It is also known that aromatic hydrocarbons can be found in the human body. In a

[12] *Citing* Schneider H., *Long Term Performance of Polypropylene Geosynthetics, "Durability and Aging of Geosynthetics, Koerner*, RM, Ed., (Elsevier 1989) 95-109.
[13] Strus, M., et al., *The In Vitro Effect of Hydrgen Peroxide in Vaginal Microbial Communities*, FEMS Immunol Med Microbiol, 2006 Oct; 48(1:56-63).
[14] *Id.*

paper from HB Moon entitled, "*Occurrence and Accumulation Patterns of Polycyclic Aromatic Hydrocarbons and Synthetic Musk Compounds in Adipose Tissues of Korean Females*," *Chemosphere* 2012 (86:485-490), these aromatic hydrocarbons were noted to be present in, "[t]otal concentrations of PAHs and SMCs in adipose tissues rang[ing] from 15 to 361 (mean:119) ngg(-1) lipid weight and from 38 to 253 (mean:106) nng(-1) lipid weight respectively…. The results of this study provide baseline information on exposure of PAHs and SMCs to the general population in Koreans."

It has also been determined that halogenated hydrocarbons can be found not only in adipose tissue but also the blood stream. A paper entitled, "*Determination of Volatile Purgeable Halogenated Hydrocarbon in Human Adipose Tissue and Blood Stream*," from the *Bulletin of Environmental Contamination and Toxicology*, Volume 23, Issue 1, pp 244 – 249 published in 1979, found halogenated hydrocarbons, pesticide by-products, both in human adipose tissues and the blood stream. In a subsequent paper from 1985 in *Environmental Health Perspectives*, Volume 60, pp. 127-131, Henry Anderson, in his paper entitled, "*Utilization of Adipose Tissue Biopsy and Characterizing Human Halogenated Hydrocarbon Exposure*," also found these pesticide by-products in human adipose tissue. Accordingly, the body location where the polypropylene mesh is being placed can expose it to known chemical degradation agents.

However, chemical degradation is not the only way that polypropylene degrades *in vivo*. In a paper from N Das in the Journal of Biotechnology Research International, Volume 2011, Article ID 941810, entitled, "*Review Article: Microbial Degradation of Petroleum Hydrocarbons Contaminant: An Overview*," found that various bacteria such as Pseudomonas species, Bacillus species, Mycobacterium and Corynebacterium species, which are present in a woman's vagina, can degrade petroleum hydrocarbons. Also fungi such as the Candida

species, also present, can degrade petroleum-based hydrocarbons.[15] Microbial agents that can be found inside the normal and abnormal flora of the human vagina such as Candida and, with certain pelvic infections such as Bacillus and Pseudomonas, can be a source of biological degradation of polypropylene products.

A paper entitled, "*Health, Safety and Environment Fact Sheet: Hazardous Substances - Plastics*," from CAW/TCA (www.caw.ca), August 2011:343, found that polypropylene degradation products and residues can form carbon monoxide, acrolein, aldehydes and acids, qualifying these health hazards as toxic and irritants. In a paper from D Lithner in 2011 at 4, entitled, "*Environmental and Health Hazards of Chemicals in Plastic Polymers and Products*," University of Gothenburg, it is stated that, "[n]on-biodegradable polymers can be degraded by heat, oxidation, light, ionic radiation, hydrolysis and mechanical shear, and by pollutants such as carbon monoxide, sulphur dioxide, nitrogen oxide and ozone. This causes the polymer to get brittle, to fragment into small pieces and to release degradation products." (Citations omitted.) Lithner continues, "[o]ther substances (besides monomers) are often needed for polymerization to occur, for instance initiators, catalysts, and, depending on manufacturing process, solvents may also be used. The resulting plastic polymer can be blended with different additives, for instance plasticizers, flame retardants, heat stabilizers, antioxidants, light stabilizers, lubricants, acid scavengers, antimicrobial agents, anti-static agents, pigments, blowing agents and fillers, and is finally processed into a plastic product. There are many different plastic polymers and several thousand different additives, which result in an extremely large variation in chemical composition of plastic products." *Id.* at 6 (citations omitted). "Since plastic products are composed of many different chemicals, and the main part of these [are] broken down into something completely different; this complicates the prediction." *Id.* at 8. "The type and quantity of degradation products formed may also be influenced

[15] Das, N., et al., *Review Article: Microbial Degradadtion of Petroleum Hydrocarbon Contaminants: an Overview*, J Biotech Res Intl, 2011, Article ID 941810, 1-13

by degradation mechanisms, presence of polymerization impurities, and surrounding factors, e.g. temperature and oxygen." *Id.* at 9. "Few studies combining leaching tests with toxicity tests have been performed on plastic products." *Id.* at 12. The available peer-reviewed literature regarding degradation/oxidation of polypropylene in the human body dates back to the 1960's and has been reported in numerous such publications.[16]

Two of the more important and salient articles regarding reported degradation in explanted surgical meshes (hernia and pelvic floor) are the Costello and Clave articles. In his paper, "*Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Implants from a Single Patient*," Prof. C Costello reported that hernia mesh made of polypropylene oxidized and degraded as a result of the metabolites produced by phagocytic cells during the body's inflammatory reaction to the mesh. High-magnification photographs showed cracking and peeling of the polypropylene fibers. Ethicon referenced this article in internal emails.[17]

Another article by A Clave, "*Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants*," also displayed high magnification photos of polypropylene fibers from explanted meshes and, in this case, the meshes were explanted from women's pelvic floor tissue.[18] The heavyweight meshes showed even greater cracking than the lower density meshes, but according to Prof/Dr. Clave, ALL 84 of the polypropylene explants examined showed degradation. Oxidation of the implanted mesh due to free radical attack through the synthesis of peroxides, superoxides and hypochlorous acid during the chronic inflammatory phase was listed as just one potential cause for the oxidative degradation

[16] Liebert, T, et al., *Subcutaneous Implants of Polypropylene Filaments*, J Biomed Mater Res. 1976 (10:939-951); Williams, D., *Review of Biodegradation of Surgical Polymers*, J Materials Sci, 1982 (17:1233-1246); Oswald, H.J., et al., The Deterioration of Polypropylene By Oxidative Degradation, Polymer Eng Sci, 1965 (5:152-158).

[17] ETH.MESH.005588123.

[18] Clave, A., *Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explants*, I Urogynecol J 2010 21:261-270.

within the "septic environment" in which the pelvic meshes are placed.

Given the information available to Ethicon in the scientific and medical literature concerning the potential for degradation of polypropylene, it is my opinion to a reasonable degree of medical certainty that Ethicon should have conducted clinically relevant testing to determine if naturally occurring conditions in the vagina could cause polypropylene to degrade and if so, what the quantity and quality of the products of degradation would be, whether they would be released into surrounding tissues and/or migrate in the woman's body, what the clinical implications for the woman would be and whether some women's bodies would react differently to the mesh and degradative process and its by-products.

Ethicon's Daniel Burkley, a Principal Scientist at Ethicon, testified that the science supported the conclusion that mesh could shrink, contract and degrade. Specifically, Mr. Burkley agreed that the risk of degradation increases when you have a severe inflammatory response with mesh implanted in a contaminated field.[19] Mr. Burkley also testified that polypropylene mesh in human beings is subject to some slight degree of surface degradation.[20] He agreed that degradation might be better understood if Ethicon studied or tested a product that is permanently implanted in women.[21] In fact, according to Mr. Burkley, Ethicon only conducted one study related to degradation and Prolene material. This study consisted of a Prolene suture implanted into dogs.[22] Mr. Burkley testified that the study and photos from the dog actually showed that the Prolene material used in TVT degraded and was still degrading after 7 years.[23]

It is now clear from Ethicon's internal documents that Mr. Burkley was incorrect when he said that Ethicon only performed one study related to degradation of Prolene. Contrary to

[19] Burkley Dep. (5/22/13) 184:17-24.
[20] Burkley Dep. (5/22/13) 206:2-11
[21] Burkley Dep. (5/22/13) 206:12-25.
[22] ETH.MESH.05453719 (Seven year data for ten year Prolene study: ERF 85-219).
[23] Burkley Dep. (5/23/13) 315:8-13.

Mr. Burkley's claim, he and other Ethicon scientists were involved in a Prolene human explant study that was conducted in 1987 which found that Prolene degrades while in the body. According to Ethicon's documents, Ethicon's scientists received 58 Prolene human explants from Professor Robert Guidon[24] which were analyzed by Ethicon's scientists using scanning electron microscopy ("SEM"). The SEM study revealed that 34 of the 58 Prolene explants (58%) were cracked. Further studies, including FTIR and melt point analysis, were conducted by Ethicon's scientists to determine the cause of the cracking observed in Prof. Guidon's explants. In a report authored by Mr. Burkley on September 30, 1987, he concluded that the Prolene explants had insufficient antioxidants to protect them from oxidation which led to *in vivo* degradation of the Prolene devices.[25] Importantly, Ethicon has not made any changes to Prolene since it was introduced to the market, except that, in 2011, they reduced the amount of Sanatanox (another antioxidant), which could potentially make Prolene more, not less, susceptible to oxidized degradation.[26] Thus, Ethicon's internal studies clearly demonstrate that Ethicon's scientists had concluded that Prolene can degrade while implanted in the human body.

Ethicon subsequently hired an outside consulting firm to resolve the cause of the erosion of its surgical meshes for the pelvic floor. In a June 22, 2011 report, PA Consulting Group informed Ethicon that, "[p]olypropylene can suffer from degradation following implant… a process which initiates after a few days post implantation in animal studies."[27] The consulting report discusses numerous images of polypropylene mesh that show "physical

[24] DEPO.ETH.MESH.00004755
[25] ETH.MESH.12831391 at ETH.MESH.1281392
[26] ETH.MESH.02589032 and ETH.MESH.07192929 (May 18, 2011 PA Consulting Report: Investigating Mesh Erosion in Pelvic Floor Repair and PowerPoint presentations
[27] ETH.MESH.02589032 and ETH.MESH.07192929 (May 18, 2011 PA Consulting Report: Investigating Mesh Erosion in Pelvic Floor Repair and PowerPoint presentation).

degradation" of the mesh.[28] In addition, in a 2009 presentation, Ethicon Medical Director Piet Hinoul stated that meshes are not biologically inert.[29]

I have personally seen mesh that is broken, cracked, brittle and look different from when it came out of the package. Interestingly, despite years of scientific literature, its own internal dog study, performed by consultants it hired, showing that degradation of mesh occurs, and even despite the fact that Ethicon's own internal risk assessments include degradation as a known risk, Ethicon's Instructions for Use (IFU) continues to claim to this day that the mesh in the TVT "is not absorbed, nor is it subject to degradation or weakening by the action of enzymes."[30] This is not simply inaccurate, but is false and misleading for all of the reasons stated above, including, most importantly, that Ethicon's own internal documents and testimony from its employees confirm that the mesh degrades.

It is my opinion to a reasonable degree of medical certainty that the mesh used in TVT degrades. The effect of chemical and biological degradation of the TVT Prolene mesh in a woman's tissues can lead to a greater foreign body reaction, enhanced inflammatory response and excessive scarring, which can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence

[28] *Id.*
[29] ETH.MESH.01264260 (Presentation, "Prolift+M," P Hinoul, MD, Ethicon Pelvic Floor Expert's Meeting – Nederland, Utrecht, May 7, 2009).
[30] May 2015 TVT IFU; ETH.MESH.02340406

in women.

Given the information available in the scientific and medical literature concerning the potential for degradation of polypropylene, it is my opinion to a reasonable degree of medical certainty that Ethicon should have conducted clinically relevant testing to determine if naturally occurring conditions in the vagina could cause polypropylene to degrade and if so, what the quantity and quality of the products of degradation would be, whether they would be released into surrounding tissues and/or migrate in the woman's body, what the clinical implications for the woman would be and whether some women's body's would react differently to the mesh and the degradative process and its by-products.

Moreover, Ethicon failed to inform physicians or patients about the potential for degradation of the mesh and the complications that could follow. In fact, Ethicon not only failed to disclose these risks to physicians and patients, it did not accurately describe these significant risks by calling them "transitory" and by putting inaccurate statements about degradation in its IFU. This is information physicians need to know in order to have a fair and proper conversation with their patients about the use of a product. Physicians rely on device manufacturers to inform them of the risks and complications associated with their products instead of downplaying them or inaccurately stating them. By not disclosing this safety information to physicians and their patients, it is my opinion to a reasonable degree of medical certainty that Ethicon failed to properly inform physicians and patients about the risks of degradation of Prolene mesh in the TVT. In addition, by failing to inform physicians, Ethicon did not provide them with an opportunity to adequately discuss these risks with their patients.

2. <u>Chronic Foreign Body Reaction</u>

The human body has a natural and fairly predictable "host defense response" to any

foreign object placed inside of it. Whether a splinter or a surgical mesh, the human body will send white blood cells to attack the invader and, if the products of inflammation cannot ward off or destroy the invader, including if the invader is anything from bacteria to prosthetic implants, the initial acute inflammatory phase is followed by a chronic inflammatory phase. Therefore, with the placement of something like a permanent surgical mesh in human tissues, there will be a chronic or permanent foreign body reaction to the implant, as well as a chronic inflammatory response by the body.[31] In fact, Ethicon Medical Directors, Piet Hinoul and Charlotte Owens, have both testified that the chronic foreign body reaction created by the body's response to mesh can cause a severe inflammatory reaction, which can cause chronic pain, nerve entrapment, erosions, dyspareunia and the need for additional surgeries.[32]

Consultants and experts in the field informed Ethicon that there would be chronic tissue reaction to its polypropylene meshes. During a 2006 meeting at one of Ethicon's facilities, Bernd Klosterhalfen, a pathology consultant expert for Ethicon, informed Ethicon that there can be a continuing reaction between tissues in the body and mesh for up to 20 years.[33] In addition, during a February 2007 meeting, Ethicon stated that there can be, "[E]xcessive FBR [foreign body reaction]> massive scar plate > more shrinkage."[34]

Internally, Ethicon's scientists agreed. Dr. Holste testified that chronic foreign body reactions occurs in Ethicon's small pore, heavyweight meshes like the Prolene mesh found in TVT.[35] In fact, Dr. Holste testified that Ethicon developed lighter weight, large pore meshes in order to minimize the complications seen with heavyweight meshes like the Prolene used in

[31] Klinge, U., et al., *Shrinking of Polypropylene Mesh In Vivo: An Experimental Study in Dogs*, Eur J Surg 1998, 164: 965-969; Klinge, U., *Foreign Body reaction to Meshes Used for the Repair of AbdominalWall Hernias,*Eur J Surg 1998, 164:951–960; Klostherhalfen,B., *The lightweight and large porous mesh concept for hernia repair*, Expert Rev. Med. Devices 2005, 2(1); Binnebosel M, et al., *Biocompatibility of prosthetic meshes in abdominal surgery*, Semin Immunopathol 2011, 33:235-243; ETH.MESH.03658577 (Biocompatibility of Ultrapro).
[32] Hinoul Dep. (4/5/12) 99:09-25; (4/6/12) 518:14-520:20; (6/26/13) 175:1-176:17;184:18-22; 328:10-24; Owens Dep. (9/12/2012) 98:11-99:07.
[33] ETH.MESH.00870466 (June 6, 2006 Ethicon Expert MeetingMeshes for Pelvic Floor Repair, Norderstedt).
[34] ETH.MESH.01218361 (Ethicon Presentation: "State of Knowledge in 'mesh shrinkage'-What do we know").
[35] Holste Dep. (7/29/13) 52:5-55:21.

TVT.[36] Ethicon employee, Christophe Vailhe, testified that there can be an excessive inflammatory reaction or foreign body reaction that would lead to mesh erosion and contraction.[37] Despite its knowledge about the problems associated with chronic foreign body reaction, Ethicon continues to use a heavyweight, small pore mesh in its TVT product.

Contrary to this scientific evidence, Ethicon informed doctors in its IFU that its TVT mesh was "non-reactive with a minimal and transient foreign body reaction," until the IFU was updated in 2010 to remove the word "transient"[38] This was despite all of the internal documents and testimony discussed above from Ethicon's Medical Affairs and Research and Development employees that chronic foreign body reaction occurs in small pore, heavyweight meshes like the Prolene mesh in TVT. Moreover, as one of Ethicon's lead engineers stated:

"the foreign body reaction is not transitory – it doesn't ever go away, but decreases over time to a minimal level."[39] That is, it is chronic. I have reviewed numerous pathology reports from my own patients and other physician's patients and pathology reports reviewed in litigations describing foreign body reactions. Hence, the mesh potentiates a chronic, long-term inflammation. This is contrary to the express language of the TVT IFU up until 2010 and, to this date, the IFU still does not state the foreign body reaction is chronic.

Even before Ethicon launched the TVT with the heavyweight, old construction mesh for sale in the United States. Ethicon knew that Prolene mesh was far from being the ideal material for use in vaginal tissues.[40] However, despite knowing this, Ethicon decided to launch the product for use in repair of anterior prolapse, in order to gain entry into the market before competitors. Ethicon also knew that doctors had expressed fears about rejection and problems with removing the mesh at a later date, fear of infection, concern that the mesh could erode into

[36] Holste Dep. (7/29/13) 51:3-53:6.
[37] Vailhe Dep. (6/21/13) 383:8-19.
[38] ETH.MESH.02340406; ETH.MESH.02340531; TVT IFU, May 2015
[39] ETH.MESH.00211259
[40] ETH.MESH.12009027

the bladder or rectum, and concern about the stiffness of the mesh and the risk of the mesh protruding through the vagina. Even knowing of these concerns regarding the use of Prolene mesh in women's vaginal tissues, Ethicon proceeded to launch the TVT with the heavyweight, 1974 old construction Prolene mesh.

For the reasons set forth above, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT creates a chronic foreign body reaction which can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

Moreover, Ethicon failed to inform physicians or patients about the potential for a severe, chronic foreign body response and the complications that could follow. In fact, not only did Ethicon fail to disclose these risks, it mischaracterized the risks by calling them "transitory" and by putting inaccurate statements about foreign body response in its IFU. This is information physicians need to know in order to have a fair and proper conversation with their patients about the use of a product. Physicians rely on device manufacturers to inform them of the risks and complications associated with its products instead of downplaying them or inaccurately stating them. By not disclosing this safety information to physicians and their patients, it is my opinion to a reasonable degree of medical certainty that Ethicon failed to properly inform physicians and patients about the risks of foreign body response of Prolene mesh in the TVT. In addition, by

failing to inform physicians, Ethicon did not provide them with an opportunity to adequately discuss these risks with their patients.

3. Infections/Bio-films

The placement of midurethral slings, including TVT, violates one of the most basic tenets of surgical teachings in that it is the placement of a permanent implant into the patient through a "clean contaminated" surgical field, *i.e.* the vagina, which is not sterile and can never be completely sterilized.

In TVT, the weave of the mesh produces very small interstices which allow bacteria to enter and to hide from the host defenses designed to eliminate them. The bacteria can secrete an encasing polysaccharide slime (biofilm), which further serves to shield the bacteria from destruction by white blood cells and macrophages.[41] The effect and consequences of biofilm is to increase the foreign body reaction, resulting in chronic infections, chronic inflammation, erosions, and mesh and scar contracture, and was well known to Ethicon, as evidenced by the testimony of Ethicon's Head of Pre-Clinical, Dr. Joerg Holste.[42]

Importantly, the biofilm actually serves as a protection for the bacteria surrounding the mesh fibers against the body's host defense response (white blood cells), which are intended to destroy foreign invaders like bacteria. Thus, the weave induces the creation of a shield against the body's defenses to the bacteria entrained in the woven mesh, inhibiting the body's ability to fight off the infective agents within the mesh. The large surface area promotes wicking of fluids and bacteria which provides a safe haven for bacteria which attach themselves to the mesh

[41] Osterberg, B., et al., *Effect of Suture Materials on Bacterial Survival in Infected Wounds: An Experimental Study*, Acta. Chir. Scand 1979, 145:7 431-434; Merritt, K., *Factors Influencing Bacterial Adherence to Biomaterials*, J Biomat Appl 1991, 5:185-203; An, Y., *Concise Review of Mechanisms of Bacterial Adhesion to Biomaterial Surfaces*, J Biomed Mater Res (Appl Biomat) 1998, 43:338-348; The TVM Group: J. Berrocal, et al., *Conceptual advances in the surgical management of genital prolapsed*, J Gynecol Obsted Biol Reprod 2004, 33:577-587.
[42] Holste Dep. (7/30/13) 295:24-298:14, 411:15-414:24.

during the insertion process.[43] Daniel Burkley testified that reducing surface area could reduce the amount of chronic inflammation.[44] Additionally, the size of the mesh placed equates to a large surface area with many places for bacteria to hide while being protected from host defenses leading to numerous complications.[45]

There have been numerous peer-reviewed journal articles regarding secondary-mesh related infections as well as the dangers of implanting surgical mesh in a clean/contaminated field. Of note, in May of 2013, at the AUA meeting in San Diego, Dr. Shah and his colleagues reported on the "*Bacteriological Analysis of Explanted Transvaginal Meshes*," which included explanted samples of both SUI slings and prolapse meshes. Of the 50 explants examined, 52% of those explanted due to patient complaints' of painful mesh were infused with pathogenic organisms, 20% of those explanted due to vaginal erosions had pathogenic organism, and 83% of those explanted due to urinary tract erosions were contaminated with pathogenic organisms.[46]

When polypropylene particles separate from the surface of the mesh fiber due to degradation, see infra, the surface area of the mesh is greatly increased thus providing even greater areas for bacterial adherence to the mesh, more elution of toxic compounds from the polypropylene, and also more of the free toxic polypropylene itself, all of which increases the inflammatory reaction and intensity of the fibrosis.[47] This cracking of the mesh surface also provides safe harbors for infectious bacteria to proliferate.

In his periodic histopathological analyses for Ethicon of its pelvic floor explants, Dr.

[43] Klinge, U., et al., *Do Multifilament Alloplastic Meshes Increase the Infection Rate? Analysis of the Polymeric Surface, the Bacteria Adherence, and the In Vivo Consequences in a Rat Model*, J Biomed Mater Res 2002, 63:765-771; Vollebregt, A, et al., *Bacterial Colonisation of Collagen-Coated Polypropylene Vaginal Mesh: Are Additional Intraoperative Sterility Procedures Useful?*, Int Urogyn J 2009, 20:1345-51.
[44] Burkley Dep. (5/22/13) 371.
[45] Klinge, *supra* n. 26; Vollebregt, *supra* n. 26.
[46] Shah, K., et al., Bateriological Analysis of Explanted TransvaginalMeshes (Abstract 1144).
[47] Jongebloed, *supra*, n. 1; Sternschuss, G, et al., *Post-Implantation Alterations of Polypropylene in the Human*, J Urol 2012, 188:27-32; Clave, *supra*, at 6.

Klosterhalfen reported to Ethicon that, in virtually 100% of those instances in which mesh had been explanted due to erosions, he found a secondary, mesh-related infection at the tissue/mesh interface.[48] Mesh exposure and erosion cause the fibers to be further exposed to bacteria that will adhere to and colonize on the mesh surface.

Ethicon employees have testified that they were aware of these biofilms forming on the surface of the mesh.[49] However, Ethicon never performed any long-term, clinical studies to determine whether the warnings given them through the peer-reviewed literature and by their own experts and consultants were accurate, namely that mesh-related infections are real; that they cause patient injury in the form mesh erosions and recurrent, late infections; and that the transvaginal implantation through and into the non-sterile, septic vagina is below the standard of care for any surgical technique, especially one used to treat non-life threatening conditions, such as stress urinary incontinence.

Therefore, it is my opinion to a reasonable degree of medical certainty that the TVT mesh is susceptible to biofilm formation due to the weave of the mesh allowing the infiltration, harboring, and protection of bacterial contaminants; the degraded mesh surface harboring bacteria; the passage through and into a clean/contaminated field; and after exposure/erosion of the mesh into the vagina or other organs, further contamination of the mesh with a multitude of vaginal flora that further increases the risk of harmful and recurrent infections in women. Accordingly, the TVT transvaginal technique, as well as the TVT mesh itself, are not safe for their intended purpose of implantation into a woman's pelvic tissues and can lead to severe complications in patients, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of the mesh, sexual

[48] ETH.MESH. 00006636.
[49] Holste Dep. (7/30/13) 283:19-284:5.

dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

Finally, Ethicon's claims in its IFU that the TVT mesh may "potentiate infection" are misleading, at best. If, by the intentionally ambiguous term, "potentiate," Ethicon means "cause," then this is true for all of the reasons stated above. If by "potentiate," Ethicon means "exacerbate an existing infection," then the statement is misleading at best. Ethicon failed to warn physicians and patients that a slimy, protective biofilm could form on the mesh leading to painful erosions, recurrent, late infections and the need for mesh removal. The TVT IFU contrasts sharply with the PROLENE IFU on this issue. The PROLENE IFU states as follows: PROLENE Mesh in contaminated wounds should be used with the understanding that subsequent infection may require removal of the material.[50]

Ethicon did not to include this risk, despite that unlike hernia mesh, TVT mesh is being implanted through a contaminated environment – the vagina. By failing to include this risk, Ethicon did not adequately warn physicians about these important risks, nor by extension, provide surgeons with an opportunity to discuss these risks with their patients.

4. <u>Pore Size and Fibrotic Bridging</u>

Fibrotic bridging occurs when the fibers surrounding the pores of the mesh are too close together to allow the tissue in the pore enough room to recover from the trauma of tissue damage due to implanting a surgical prosthetic device. Pores that are large enough for good, newly- vascularized tissue tend to be filled with fatty tissue versus small pores that become

[50] ETH.MESH.02342102.

filled with scarred or fibrotic tissue. In those instances, the scar forms across the pores or "bridges" from one side of the pore to the other. This can occur either due to the granulomas around the mesh fibers joining together or due to densely-formed fibroblasts between these granulomas. Either way, such bridging can lead to the creation of a rigid, scar plate that can encapsulate the mesh with scar tissue. Simply put, small mesh pores that cause fibrotic bridging turn the mesh into a solid sheet of scar tissue and there is no space or room for tissue to grow into the mesh, which is the intended purpose of the mesh. The fibrotic bridging and scar plate prevents tissue in-growth and causes complications, including, among other things, pain with the rigid mesh, shrinkage or contraction of the mesh, erosions due to mechanical irritation in the tissue of a rigid, scar- plated mesh, nerve entrapment, chronic pain and dyspareunia.

This concept is best illustrated by a DVD produced by Ethicon which features an Ethicon consultant, Dr. Todd Heniford, talking about a heavyweight, small pore mesh called Marlex used for hernia repairs.[51] The Prolene mesh used in TVT is of heavyweight, small pore construction and, in fact, is even heavier than Marlex. Ethicon Scientists have acknowledged that the Marlex mesh in the video is similar to the Prolene in TVT in that is heavy weight small pore mesh.[52] Ethicon has also relied on the works of Dr. Heniford relating to lightweight mesh and cited to his works in their marketing materials and professional educational materials for pelvic mesh products. Moreover, Ethicon relied on science and information regarding hernia meshes to claim the safety and efficacy of their pelvic mesh products to regulatory bodies. At least one medical director at Ethicon, Dr. Thomas Divilio, has described the work done by Dr. Heniford and others as "material science" that would apply

[51] Heniford, B.T., 2007, *The benefits of lightweight meshes in Ventral Hernia Repair in Ventral Hernia Repair*, Video produced by Ethicon.

[52] ETH.MESH.05918776 (5/04/04 Email from Schiaparelli, Jill, Strategic Grown Subject: Marlex Experience); Batke Dep. (8/01/13) 87:12 - 88:10, 113:3-114:3, 257:23-259:13; Holste Dep (7/29/13) 51:3-53:6, 55:22-57:4; Vailhe Dep. (6/20/13) 182:2 185:5.

to both hernia and pelvic mesh products. In my opinion this the video, as well as other science and information regarding hernia meshes and other pelvic meshes of particular relevance when discussing the TVT mesh as Ethicon chose to move to large pore, light weight meshes in these areas, but not for TVT.

In the video, Dr. Heniford talks about the dangers of heavy weight, small pore meshes.[53] In fact, Dr. Heniford states, "there is no excuse for using heavy weight, small pore meshes in the human body."[54] I have explanted numerous TVT and TVT meshes and have witnessed meshes with extensive scar plating and mesh encapsulation similar to the hardened/stiffened mesh viewed in the Heniford video. In numerous emails, Ethicon employees discussed concerns regarding fibrotic bridging.[55] They have testified that the heavy weight, small pore type of mesh in the TVT can lead to an increased risk of foreign body reaction, contraction of the mesh, nerve entrapment, erosions and chronic pelvic pain.[56] In other emails, when discussing these concepts, Ethicon's World Wide Marketing Director for General Surgery, Marty Chomiak, states that "… we want to avoid 'bridging', therefore we think large pores are better than small . . ."[57] Ethicon also had information and scientific knowledge regarding superior mesh designs to prevent fibrotic bridging and scar plating. Specifically, Ethicon also had scientific knowledge that light weight, large pore mesh could decrease the likelihood of foreign bodyreaction, fibrotic bridging and scar plating.[58]

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[53] Heniford Video, supra, n. 46.
[54] *Id.*
[55] ETH.MESH.04037600 (Innovations in mesh development); ETH.MESH.05920616 (7/20/07 ; Emails from Chomiak, M. to Batke, B., et al. re Defining light weight mesh); ETH.MESH.05585033 (Boris Batke Presentation – Project Edelweis – Ultrapro); ETH.MESH.05446127 (3/13/2006 Emails from Holste, J. to Engel, D., et al re Mesh and Tissue Contraction in Animal – "Shrinking Meshes?); ETH.MESH.05475773 (2/09/2007 Boris Batke, Ethicon R&D, Presentation: *The (clinical) argument of lightweight mesh in abdominal surgery*); ETH.MESH.04015102 (3/1/12 Email from Batke, Boris to Mayes, C. re AGES Pelvic Floor Conference-Gala Dinner Invitation); ETH.MESH.04037600 (3/15/12 Boris, B. PowerPoint Presentation, *Innovations in Mesh Development*,Melbourne AGES 2012).
[56] Batke Dep. (8/1/13) 87:12-88:10, 113:3-114:3, 257:23-259:13; Holste Dep. (7/29/13) 51:3-53:6, 55:22-57:4; Vailhe Dep. (6/20/13) 182:2-185:5.
[57] ETH.MESH.05920616 (7/20/07 Email from Chomiak,M. re Defining LightWeightMesh).
[58] Batke Dep. (8/1/13) 87:12-88:10, 113:3-114:3, 257:23-259:13; Holste (7/29/13) 51:3 - 53:6, 55:22 - 57:4; Vailhe

Despite having clinical knowledge of the importance of pore size to successful outcomes, and dozens of emails about the importance of pore size, Ethicon's person most knowledgeable about pore size testified that Ethicon does not manufacture its mesh to a specific pore size. Dan Smith testified as follows:

> Q: Does Ethicon have a validated test method to determine the pore size of its TVT mesh?
> A: We determine the pore size by courses and wales and that is how it's done. So the courses and wale count is a validated test method.
> Q: And I'm talking about pore size. Does Ethicon have a validated test method to determine its pore size for its mesh?
> A: The construction of the mesh is -- does not have a pore size requirement.[59]

In fact, Ethicon does not even have a test to measure the pore size of its mesh. Dan Smith testified:

> Q. Mr. Smith, does Ethicon have a validated test to describe the pore size of its TVT meshes microns? Yes or no.
> A. No….[60]

Despite this information that it did not measure pore size or manufacture its mesh to a specific requirement, Ethicon repeatedly stated in advertising and marketing materials that its mesh was "large pore." For example, in one brochure, Ethicon promotes the mesh used in the TVT family of products (including TVT) as the "Largest pore size" of any of its competitors, listing the size as 1379 um.[61] However, given that Ethicon has no verified methodology to measure pore size, Ethicon had no scientific basis upon which to base these statements. In fact, in internal documents, Ethicon scientists described PROLENE mesh as small pore: "Standard Mesh PROLENE small pores area weight 105 g/m2."[62] One Ethicon Engineer measured a mesh and determined that there were two pore sizes in the mesh, a "major" and "minor" pore. "There are two distinct pore sizes in

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Dep. (6/20/13) 182:2-185:5.
[59] Smith Dep. (2-3-14) 729:1 to 729:12.
[60] Smith Dep. (2-3-14) 779:5 to 779:8.
[61] ETH.MESH.00349508 at 9510.
[62] ETH.MESH.04941016.

the PROLENE 6 mil mesh (TVT). The major pore is about 1176 um…. The minor pore is about 295 um."[63] Certainly, neither of these pores was 1379 um, and the minor pore was substantially smaller.

In addition, the pore size of a mesh can change when the mesh is put under stress such as when a sheath is removed or the mesh is tensioned. Dan Smith agreed that these stresses can make an effective pore size smaller than 1 mm.

> Q. You would agree, Mr. Smith, that if the measurement across the pores we're looking at here -- let's assume you measure across one of those pores and let's say it's more -- let's say it's 1 millimeter across hypothetically. If a load is put on the mesh and it changes the pore size, that pore could be, after a load is put on it, under 1 millimeter; correct?
> A: It's possible depending on the load.[64]

Ethicon engineer Christophe Vaihle testified that "excessive tension on the mesh would lead to the decrease in pore size that can lead to poor tissue integration . . . ."[65] Ethicon has done nothing to change the mesh and continues to promote and sell the product with the same, heavy weight, thick filament "Old Construction 6 mil" mesh that they have been selling since 1974 (Prolene), despite what Ethicon considers to be "revolutionary" advancements in polypropylene mesh design that it brought to other pelvic floor polypropylene mesh products.[66] In summary, for the reasons set forth above, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT causes fibrotic bridging in the body, resulting in an increased inflammatory response leading to a multitude of injuries, including the possibility of multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, dyspareunia that can be chronic, nerve injury, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal

[63] ETH.MESH.00584175 (Ex. T-3583); ETH.MESH.00584179 (Ex. T-3581).
[64] Smith Dep. (2/3/2014) 816:5 to 816:15.
[65] Vailhe Dep., (6/20/13) 224:10-226:21.
[66] ETH.MESH.03905968; *see also* Prolift +M CER ("As the mass of a mesh implant is reduced and the pore size is increased, the surface area exposed to the host is reduced, and the foreign body reaction to the implant is reduced.").

scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

Moreover, Ethicon did not inform physicians and patients that its mesh was susceptible to fibrotic bridging. Ethicon failed to warn physicians and patients that fibrotic bridging could occur leading to painful erosions, recurrent, late infections, nerve injury and the need for mesh removal. By failing to do so, Ethicon did not adequately warn physicians about these important risks, nor by extension, provide surgeons with an opportunity adequately to discuss these risks with their patients.

5. Mesh Contracture/Shrinkage

Mesh contracture or shrinkage is an event that takes place after the implantation of mesh and relates to the wound healing process that occurs after the surgical trauma of implanting a foreign body made of polypropylene in the sensitive tissues of the vagina and pelvis. By 1998, polypropylene mesh was known to contract or shrink 30-50%.[67] These findings were later confirmed in numerous papers, such as those by W. Cobb and his colleagues – one of whom was Dr. Henniford (referenced above).[68] This also showed that heavier weight meshes like TVT led to greater amounts of contraction. The works of Cobb and Klinge/Klosterhalfen have been referenced in numerous Ethicon documents. Contraction or shrinkage has been shown to draw nerves close to the midurethral sling mesh both in the transobturator application[69] and for retropubic application.[70] Furthermore, contraction or

[67] Klinge, U, *Shrinking of Polypropelen Mesh in Vivo: An Experimental Study in Dogs*, Eur J Surg 1998, 164:965-969.
[68] Cobb, W., et al., *The Argument for Lightweight Polyropylene Mesh in Hernia Repair*, Surgical Innovation 2005, 12(1):T1-T7.
[69] Corona, R., et al., *Tension-free Vaginal Tapes and Pelvic Nerve Neuropathy*, J Min Invas Gynecol 2008, 15:3, 262-267; Parnell, B.A., et al.,*Genitofemoral and Perineal Neuralgia after Transobturator Midurethral Sling*, Obstet. Gynecol 2012, 119:428-431; Jacquetin, B, *Complications of Vaginal Mesh: Our Experience*, Intl Urogyn J, 2009,

shrinkage is closely related to the pore size and weight of the mesh. Small pore, heavy weight mesh leads to fibrotic bridging which leads to scar plates, mesh encapsulation and shrinkage or contraction of the mesh, which is compounded by the shrinkage effect associated with the normal wound healing process already occurring in the tissue.

This phenomenon of shrinkage and its relation to the design of the pores as well as the consequences to the patient were illustrated in an email by Ethicon Scientist Joerge Holste in a March 13, 2006 email discussing a paper he authored entitled "Shrinking Meshes?"[71] In his email, Dr. Holste states "this was our scientific statement on mesh shrinkage: Basically, small pores, heavy weight meshes induce more fibrotic bridging tissue reaction causing more mesh shrinkage during maturation of the collagenous tissue. See my presentation about biocompatibility."[72] In addition, in a presentation by Boris Batke, Associate Director R&D, he states heavier-weight polypropylene mesh results in mesh contraction of 33%.[73] In an email dated November of 2002, related to a discussion of mesh used in a TVT product, Axel Arnaud, one of Ethicon's medical directors, used 30% shrinkage of the mesh as a "rule of thumb."[74] At an Ethicon expert meeting in Norderstedt, Germany in 2007, an Ethicon employee presented a PowerPoint entitled "Factors Related to Mesh Shrinkage" in which all of these issues were clearly laid out.[75]

Mesh shrinkage was known by Ethicon as early as 1998 in published work by Ethicon's

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20:893-6; Tunn, R, *Sonomorphological Evaluation of Polypropylene Mesh Implants After Vaginal Mesh Repair in Women with Cystocele or Rectocele*, Ultrasound Obstetrics Gynecol 2007, 29:449-452.

[70] Heise, C.P., et al., *Mesh Inguinodynia: A New Clinical Syndrome After Inguinal Herniorrhaphy?*, J Am Coll Surg.

[71] ETH.MESH 05446127, *supra*, n. 34.

[72] *Id.*

[73] ETH.MESH 05479717 (3/1/11 Boris Batke, Ethicon Associate Director R&D, Presentation: Ethicon PolypropyleneMesh Technology).

[74] ETH.MESH 03917375.

[75] ETH.MESH. 02017152 (Nordestadt Expert's meeting 2007); ETH.MESH.01782867 (Factors Related to Mesh Shrinking).

then consultants, Uwe Klinge and Bernd Klosterhalfen.[76] They noted in these early papers that all polypropylene meshes shrink 30-50%. This was restated in later works by W Cobb and his colleagues[77]--one of which was Dr. Heniford (referenced above). The words of Cobb and Klinge/Klosterhalfen have been referenced in numerous Ethicon documents and thus, Ethicon was well aware of these findings regarding the shrinkage or contraction of polypropylene meshes in vivo. Ethicon was further aware that heavier weight meshes led to greater amounts of contraction. And, notably, Ethicon equated the tissue reaction in the abdomen to heavyweight mesh to the tissue reaction in the pelvis to heavyweight mesh in marketing materials, professional educational materials and regulatory materials.

It is my opinion to a reasonable degree of medical certainty that as a result of work with internal and external experts and consultants in the late 1990s, multiple internal documents and articles, and the scientific literature as a whole, that Prolene mesh used in TVT not only could, but would shrink and contract, and that this shrinkage could lead to painful complications in women implanted with TVT, such as multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, nerve injury, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others.

As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women, and Ethicon failed to warn physicians and patients of the possibility of shrinkage and

[76] Klinge U, Klosterhalfen B, Muller M, Ottinger A, Schumpelick V. Shrinking of Polypropylene Mesh in vivo: An Experimental Study in Dogs. Eur J Surg. 1998: 164; 965-969

[77] ETH.MESH.07455220.

contraction and the adverse outcomes that could occur as a result.

6. Fraying, Particle Loss, Roping and Curling, Deformation and Loss of Pore Size

Ethicon designed the TVT mesh such that, when stress was put on the mesh, particles would separate from the mesh – this was called fraying or linting.[78] One of Ethicon's engineers described this as a "defect" that resulted from the method of cutting the mesh: "The mesh frayed is the reverse defect of the mesh features (elasticity of the mesh is one of the commercial arguments to market the TVT)…. [T]he root cause of this phenomenon are known: the way to cut the mesh (blade cutting). If we change the way to cut the mesh (ultrasonic cutting or laser cutting) it seems we can limit the mesh frayed defect significantly…."[79]

As early as 2000, Ethicon's engineers documented that particles from TVT Prolene mesh fell into women's tissues as a result of the tape edges being damaged during sheath removal.[80] In April 2001, Dr. Alex Wang, "one of the most experienced TVT users in the world," reported problems with frayed mesh and uneven tape width.[81] Although the issue was described as "serious" and as requiring "urgent attention and solution," Ethicon Medical Director, Dr. Martin Weisberg, simply concluded that the deformity in the mesh would be unlikely to have any clinical significance. Dr. Weisberg testified that although he did not actually know whether frayed mesh leading to particle loss would have clinical implications, he does not recall whether he or anyone else at Ethicon studied the issue.[82] Just a few months later, however, Ethicon received a complaint by an experienced surgeon regarding a patient

[78] Weisberg Dep. (5/31/13) 461:7-462:3 ("Q. So engineers within the company knew that fraying of the product was inherent in the design? A. Yes.").
[79] ETH.MESH.01813975 at 2 (Ex. 3160/3587).
[80] ETH.MESH.01317515 (7/12/00 Preventia TVT-2 Risk Analysis Procedure/Tensioning Frayed Mesh/Particle Loss). at 7523.
[81] ETH.MESH.03905472 (6/4/01 Emails from Wang, A. re TVT Recommendation for Ethicon Study of Fraying/Particle Loss).
[82] Weisberg Dep. (5/31/13) 469:23-470:16.

who experienced vaginal wall erosion following a TVT procedure which was first noted by her husband during intercourse.

According to the surgeon, "the tape appeared frayed and tiny fibers were protruding through the vaginal wall."[83] In November 2003, Dr. Weisberg reported that there had been a total of 58 complaints of fraying with TVT since introduction of the device in 2000. He observed that the following occurs when the mesh frays: "[T]he mesh elongates in places; the mesh narrows in places; and small particles of Prolene might break off … and that [s]tretching of the mesh increases the probability of fraying."[84] Once again, however, Dr. Weisberg concluded that "since fraying does not affect the safety and efficacy of the TVT device, it has been determined not to pursue any corrective actions at this time."[85] Dr. Weisberg confirmed during his deposition that no corrective action was taken and, although he did not know whether Prolene particles could elicit a chronic foreign body response, he does not recall whether he or anyone else at Ethicon investigated the issue.[86]

In 2004, Ethicon continued to receive complaints from surgeons about fraying and "brittle" mesh and particles falling into the operating field.[87] One of the company's "most urgent customers," Swiss surgeon Dr. J. Eberhard, wrote the following: "Already at the operation it is embarrassing to see how the tape is crumbling. But it gets worse if there is stretch on the tape.… I can't understand that no one will solve that problem for such a long time. As the latest, as the tape has becoming blue, everyone has realized that the quality of the tape is terrible."[88]

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[83] ETH.MESH.02621559 at 2276 (Ethicon Issue Report TVT Retropubic 2001 Open Date Between 01- Jan-2001 and 31-Dec-2001).
[84] ETH.MESH.00541379 (11/18/03Memo fromWeisberg re Mesh Fraying for TVT Devices Inadequate Testing).
[85] *Id.*
[86] Weisberg Dep. (5/31/13) 469:23-470:16.
[87] ETH.MESH.00863391 at 3392 (2/27/04 Emails from Smith, D. re 2 TVT Complaints Concerning Allegedly Brittle Mesh).
[88] ETH.MESH.02180833 (11/12/04 Letter from Prof. Dr. Eberhard (translated)); ETH.MESH.02180828 (11/12/04 Telefax from Sibyll, B. re Prof. Dr. Eberhard).

Dan Smith, the Lead Engineer on TVT lamented the particle loss that was revealed when the mesh was dyed blue: "This is not going away anytime soon and competition will have a field day, major damage control offensive needs to start to educate reps and surgeons UPFRONT that they will see BLUE shit and it is OK."[89] Indeed in November 2004, one of the "top 3 complaints" included "Mesh frayed."[90] Once again, however, Ethicon decided to take no corrective action.[91] Instead, sales representatives were instructed to reassure their doctors that, "Prolene is proven to be inert," the "particles will not cause any problem," and to "be proactive" because "the competition will try to target this!"[92] Physicians were told the particles are "non- reactive" and that fraying does not affect the safety or efficacy of the device.[93] In fact, it has consistently been Ethicon's position that frayed mesh and resulting particle loss as well as roping, curling and deformation of the mesh do not create a safety risk and have no clinical significance.[94]

However, as noted above, Ethicon never tested whether the particles would cause pain in women.[95] Moreover, Ethicon never specifically tested whether the particles, or frayed, curled shrunken and deformed mesh, would cause pain when in close proximity to the pelvic and vaginal nerve bundle and muscles. An independent investigator, Dr. Pariente, did and published a study that concluded that "the very high particle shedding for both Sparc (AMS) and TVT (Ethicon) may be of significant long term clinical concern in some quarters."[96] In addition, Ethicon collected data from physicians who informed Ethicon that particles could,

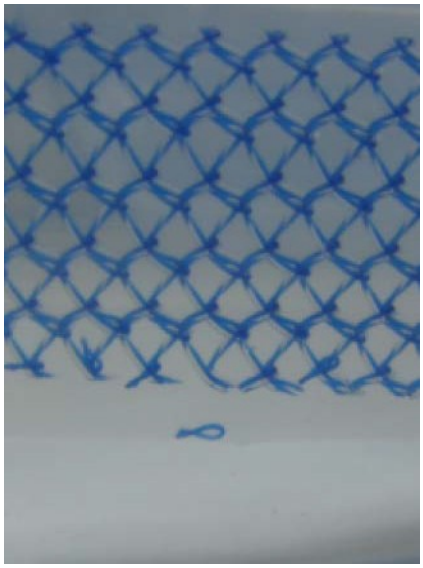
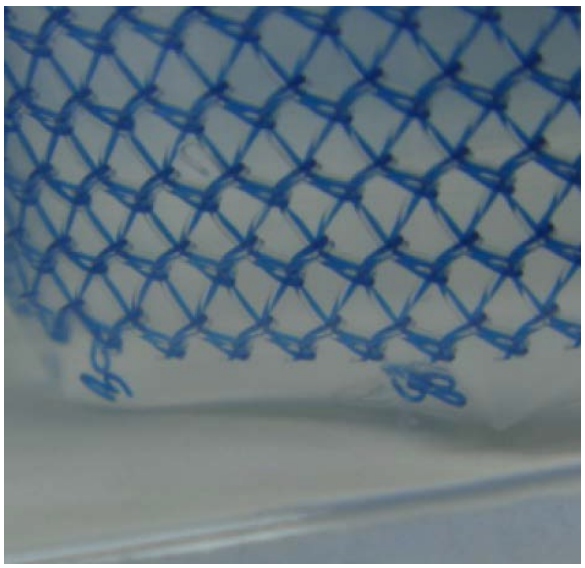
[89] ETH.MESH.00863391.
[90] ETH.MESH.01813975 (Ex. T-3160 / T-3587).
[91] ETH.MESH.02180826 (11/12/04 Email fromMenneret, D. re Mesh Fraying: Dr. Eberhard Letter).
[92] ETH.MESH.00865322 (3/2/04 Email from Bell, S., Ethicon Marketing Director Europe to Sales & Marketing Team re Reminder on Blue Mesh – Frayed Mesh/Particle Loss).
[93] ETH.MESH.03535750 (10/12/2005 Hunsicker, K., Ethicon Clinical Operations Regional Manager, Presentation: *Investigator Initiated Study Process – Inadequate Testing*).
[94] ETH.MESH.00541379, *supra*, n. 58; ETH.MESH.00858252 (2004 Memo from London Brown, A. re Mechanical Cut v. Laser Cut Mesh Rationale).
[95] Trial Testimony of Piet Hinoul, Batiste v. Ethicon, page 26-28.
[96] ETH.MESH.01221055 (Pariente, J-L, *An independent biomechanical evaluation of commercially available suburetheral slings*, Issues in Women's Health 2003).

indeed, cause pain and dyspareunia.[97] Moreover, Ethicon medical director Piet Hinoul testified the particles that fall of the mesh create inflammation and inflammation can cause pain.[98] Although Ethicon claims that its own internal testing shows approximately 1% particle loss with TVT,[99] Dr. Pariente's study demonstrated TVT particle loss as high as 8.5% - 10 times higher than most of its competitors.[100] In addition, Ethicon's April 2006 Clinical Expert Report on Laser Cut Mesh suggested there was a decrease in particle loss with laser cut mesh and this "decrease would lead to less non-functioning material left in the tissues."[101] It cannot be disputed that the greater the nonfunctioning material left in a patient's tissues, the greater the surface area of polypropylene the patient is exposed to, and the greater the inflammatory responses and the greater the foreign body response. As discussed above, the long term consequences of this chronic foreign body reaction and inflammatory response can be, among other things, chronic pain, lifelong risk of erosions, dyspareunia and failure of the device. If the individual flakes work their way through the vaginal mucosa, this can lead to dyspareunia and/or painful intercourse for the partner as noted in the complaint received by Ethicon back in 2001 referenced above. The larger the surface area the greater the risk associated with vaginal mesh. Finally, detached flakes of polypropylene may migrate into the vasculature or lymphatics and cause problems remote from the pelvis. For these reasons, Ethicon should have used a mesh without a fraying and particle loss defect when selling its TVT for permanent implant in a woman's vaginal tissues.

Ethicon continued to receive complaints related to particle loss from the mechanically cut mesh in the TVT. In 2010, customers complained that they were seeing pieces of mesh in

[97] ETH.MESH.05644163 at 4166 (Dr. Hilton, one of Ethicon's principal investigators in the TVT v. Burch trial, informed Ethicon that: "The small particles migrate and cause pain during intercourse.").
[98] Trial Testimony of Piet Hinoul, Batiste v. Ethicon, page 26-28.
[99] ETH.MESH.000585802; ETH.MESH.00585842; ETH.MESH.00585823 06/27/06 (Email from Kammerer, G. re GY: ***URGENT*** French STANDARD ON TVT & MESHES (COMMENTS REQUIRED)).
[100] ETH.MESH.01221055, *supra*, n. 67; ETH.MESH.00585842 (6/12/06 Email from Kammerer, G re TVT LCM –
[101] ETH.MESH.00167104 at 7109.

the unopened packages. Ethicon employees initially responded that "No, this is not nor do we recommend using the product." Pictures from Ethicon's complaint file reveal particles of the mesh that have begun to break off from the mesh inside the package. [102]

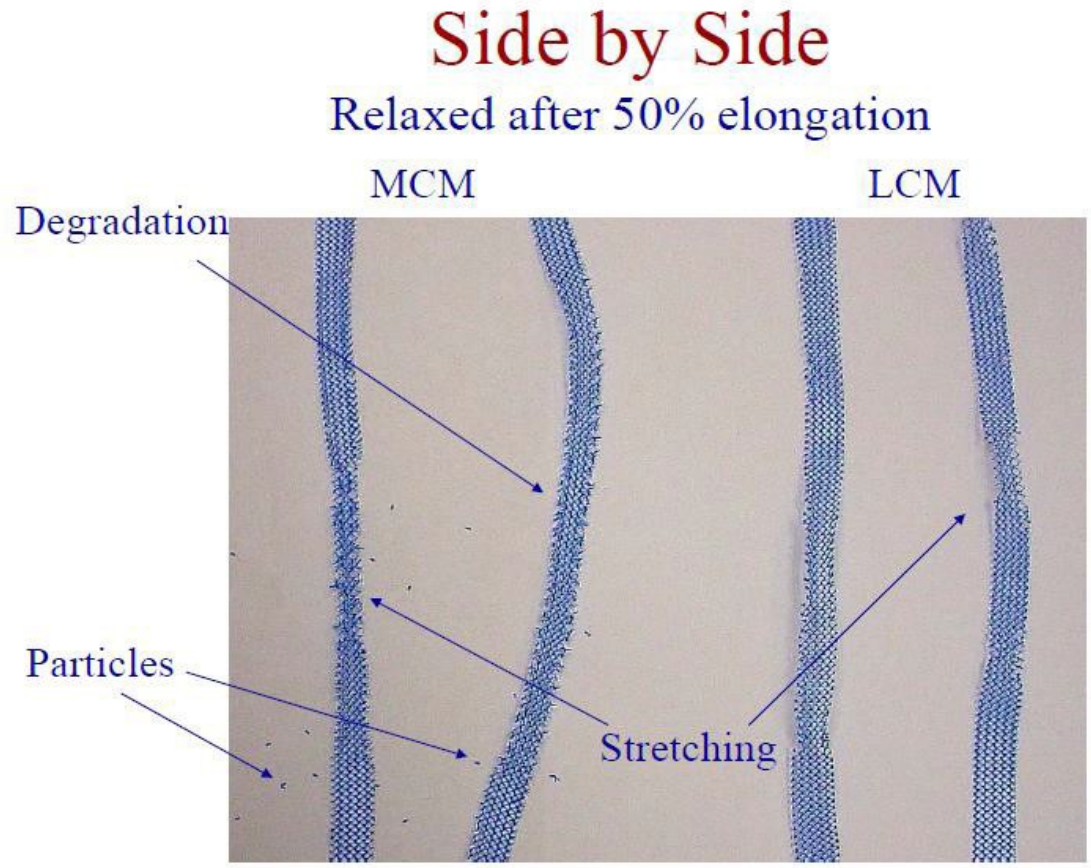
Nine packages with particles of lose mesh were returned to Ethicon for analysis. I have requested to examine these products, but have been told that Ethicon has discarded these products.[103] Ethicon employees later reversed their position on the mesh particles stating that: "mesh particles of this size are common with the manual cutting process and are within our specifications. The product is safe to use."[104] This conclusion seems to be at odds with internal manufacturing documents indicating that nearly 2,000 TVT and other mesh products were rejected because of foreign matter in the product or packaging during the month of March, 2010 alone at Ethicon's Neuchatel manufacturing facility.[105] Ethicon's conclusion that the products were safe to use does not appear to be a result of any scientific or engineering study of the returned products,

[102] ETH.MESH.13204508.
[103] Letter from Ben Watson to Andrew Faes, April 16, 2015; Letter from Andrew Faes to Ben Watson, March 25, 2015.
[104] ETH.MESH.13226457.
[105] ETH.MESH.13907354-55.

but rather the conclusion of Ethicon Medical Director David Robinson that "…the possibility for the tiny tape fragments observed… … to cause adverse consequence in a patient… … should be considered remote. The presence of tiny tape fragments in the product package is not expected to change the product safety profile."[106] It is my opinion to a reasonable degree of medical certainty that this conclusion is incorrect and not supported by any study or clinical evidence gathered by Ethicon. In fact this conclusion is belied by the fact that Ethicon told the same physicians who complained about the particles that they may wish to consider TVT mesh manufactured with a laser cutting process that does not result in tiny mesh particles within the package.[107] Because of dangers associated with loose particles, fraying and deformed mesh, described more fully below, the mesh from this TVT mesh posed unreasonable dangers to women and Ethicon should have never allowed the mechanically cut mesh in the TVT to be offered for sale for implantation in women. In addition to fraying and particle loss, the mechanically cut meshes used in TVT has also been shown to rope, curl and deform when under tension. In 2006, an Ethicon Engineer, Gene Kammerer, made a presentation that clearly showed each of these defects in the mechanically cut mesh. These photos clearly show particle loss, fraying, degradation, roping

and deformation when the mechanical cut mesh was stretched and compared to TVT Laser Cut.[108]

[106] ETH.MESH.04101014.
[107] ETH.MESH.13226457.
[108] ETH.MESH.08334245.



As noted these photos show mesh after 50% elongation. I have read depositions of Ethicon personnel claiming this is not a realistic elongation seen with mesh. However, Ethicon's engineer who took the photos, Gene Kammerer, explained that he had experienced it himself in testing:

> The link between the elongation percent, not force, and the integrity of the mesh is this. During the operative procedure as the surgeon removes the protective sheath from the mesh, the mesh stretches or elongates. It is my experience, after viewing many surgical procedures and performing numerous procedures on cadavers myself, that the mesh stretches approximately 50% at the maximum. There is also additional stretching that occurs if the surgeon elects to do an adjustment on the position of the mesh under the urethra. It is these two occurrences which produce the majority of the particle loss and loss of the integrity of the construction of the mesh.[109]

Again, Ethicon claimed that these problems with the mesh did not have any clinical

[109] ETH.MESH.00584811.

significance despite the fact that surgeons were complaining.[110] However, Ethicon's own internal documents demonstrate that this is not true. According to Ethicon's Failure Modes documents, the loss of pore size due to mesh narrowing or deformation can lead to urinary retention or erosion. Ethicon's own dFMEA from 2006 shows that the hazards of curling/roping, frayed edges and inadequate pore size of mesh can lead to the harms of erosion, recurrence, and pain.[111]

When discussing the dFMEA for Laser Cut Mesh, Former Medical Director, David Robinson, agreed that pore size of both the Laser Cut and Mechanically Cut mesh "[c]ould reduce, the tissue might not encapsulate . . . the tissue might not grow through the mesh. It can become encapsulated and then it could cause . . . a rejection of the mesh."[112] And, Dr. Robinson testified that rejection of the mesh can lead to erosion.[113] These changes in the mesh may lead to erosion or pain for women with the deformed mesh implanted in their bodies. Further, according to Ethicon, this curling, roping or narrowing of the mesh may also cause urinary retention in addition to erosion and pain.[114]

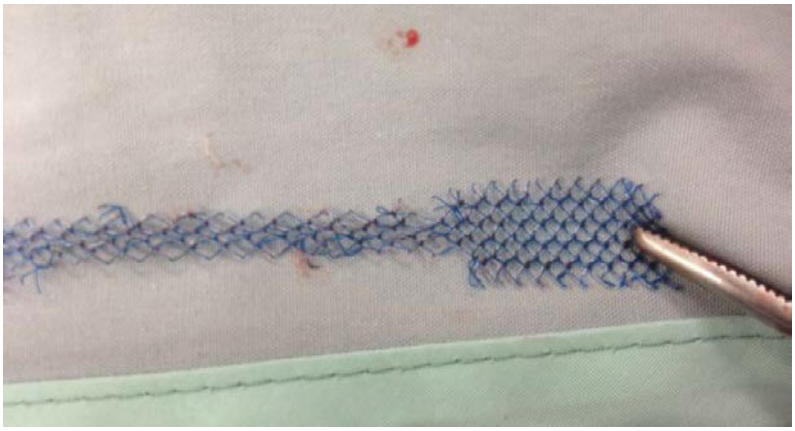
In fact, I have witnessed the same type of roping and narrowing of TVT when I placed them myself. I see the deformed and roped mesh when I remove them. This localized pressure under the urethra leads to complications like, among others, urinary retention, chronic pain, dyspareunia and erosions. In addition, I have reviewed Ethicon TVT training videos that show the exact problem discussed about related to deformation and roping of the "tape" under the urethra.[115] Finally, according to Ethicon's Dan Lamont, it chose to continue to sell "mechanically cut mesh despite knowing that it had the potential for degradation, particles

[110] ETH.MESH 00440005; ETH.MESH 00302390 (TVT-Base & TVT Review for Laser Cut Mesh (LCM) Risk Analysis).
[111] ETH.MESH.01218019.
[112] Robinson Dep. (9/11/13) 1070:23-1072:25.
[113] *Id.*
[114] Robinson Dep. (9/11/13) 1079:3-4-1081; 1081:9-13; 1083:8-18; ETH.MESH.01218019.
[115] ETH.MESH.PM.000004 (TVT Retropubic Implantation Video).

floating around in women's bodies, stretching, and roping . . ."[116] Lamont admitted that the fraying of the mesh was a "defect" of the mesh.[117]

Not surprisingly, Ethicon continues to receive complaints related to the mechanical cut mesh used in TVT fraying, roping and curling. Recently, the highest volume user of TVT products in Canada, Dr. Kenny Maslow, complained to Ethicon that the mesh used in TVT would fray down to a thin fiber even with "very little tension applied to the sling."[118]

Dr. Maslow included a picture of the frayed mesh used in TVT when he reported the issue to Ethicon.



[116] Lamont Dep. (9/11/13) 30:18-24.
[117] Lamont Dep. 9/11/13) 15:16-16:10.
[118] ETH.MESH.12910023.

Another feature of mechanically cut mesh is its sharp edges as shown on this photo:[119]

While Ethicon states that these sharp edges are part of the intended "velcro" effect of mesh, it was a feature about which Ethicon had received complaints tied to injuries and erosions. For example, during on market research test with physicians, it was reported:

> The surgeon felt that the MCM strips was elastic but with "hairs" on the edges and that it scratched with abrasive texture scraping (like the Scotch -BriteTM pads), furthermore a lot of particles were released and a rope/string effect could occurred if an excessive force was applied.[120]

In fact, when one agency recognized a spike in erosions, it inquired whether this was a result of "the cut ends of the tape appear to be sharper and more likely to cut tissue."[121] A sentiment shared by some physicians and reported to Ethicon:

> Basically, he thinks that erosions due to the TVT mesh are underestimated in reports. The reason is that in order to recognize them, a very careful vaginal examination is needed. Most of the time, a "hidden" erosion is asymptomatic and neither the patients nor their sexual partner if any complain. But it might happen that a patient may complain. He believes that erosion are due to the

[119] ETH.MESH.09656795.
[120] ETH.MESH.06696589.
[121] ETH.MESH.00330760.

> sharp edges of the mesh. He wanted to suggest that we add to the mesh edges a kind of seam that would help preventing erosion.[122]

Dr. Axel Arnaud responded that Ethicon did not want to modify its mesh (even if it caused erosions) because Ethicon did not want to lose the marketing edge of using the Ulmsten/Nilsson data. He wrote:

> I also indicated that we want to be very careful with any modifications of our tape since a change in the mesh would obsolete all the long term clinical results we have about the procedure.[123]

However, the market pressure on Ethicon to create a laser cut mesh without particle loss, roping and deformation became very strong. Paula Evans, Gynecare European Marketing Manager, described the situation as "France is in a recovery mode, Germany is hemorrhaging business … Without laser cut, there is the real risk that more business will be lost."(sic)).[124] Hence, the laser cut mesh project went forward presumably in an effort to address the chronic problems with particle loss, fraying, sharp edges and elongation seen with mechanically cut mesh.[125]

During early development of laser cut, Ethicon acknowledged that mechanical cut mesh and laser cut mesh were two separate mesh products and to imply otherwise would be misleading. In December 2005, Kevin Mahar described the marketing strategy "…KEEP selling regular TVT (the 'Colonel's Original Recipe') to those customers that want/love it…and KEEP going forward with 8 years of data, etc with the original recipe … We do not mislead them that this is the same product…"[126] In discussing that document, Dr. Robinson verified that Mahar was referring to the mechanically cut mesh as the Colonel's Original

[122] ETH.MESH.03911107 (Axel Arnaud reporting his interview with Professor Hausler).
[123] *Id.*
[124] ETH.MESH.04985249.
[125] ETH.MESH.00301741 (11/21/05 Email from Lamont, D. re !!!!GREAT NEWS FOR TVT LASER CUT MESH!!!! –Frayed mesh/particle loss); ETH.MESH.00394544 (2/01/06 Global Regulatory Strategy – GYNECARE TVT – Laser Cutting Project);Weisberg Dep. (5/31/13) 487:13-488:7.
[126] ETH.MESH.00687819 (Ex. T-3164).

Recipe:

> Q: He writes, "While we" -- "While we would work with our agency to get this right, my thoughts are that we keep selling regular TVT," meaning the mechanically-cut mesh, right?
> A. Yes.
> Q. "(The Colonel's 'Original Recipe') to those customers that want/love it." Right?
> A. Yes.
> Q. Talking about a piece of plastic that is permanently implanted in a woman's body as the "Original Recipe," right?
> A. That -- yes, that's correct.[127]

Ethicon initially decided that particle loss, elongation curve and flexural rigidity data on laser cut would not be required because they were not "critical to quality." In fact, this news was celebrated as "!!!!!GREAT NEWS FOR TVT LASER CUT MESH!!!!" and "less work for all of us."[128] However, because Ethicon wanted to continue to claim the marketing benefit of the Ulmsten/Nilsson series, marketing determined that some testing was needed. This was described as a way to protect the "clinical heritage" of the mesh:

> Marketing Need: Keep clinical heritage intact…. In order to continue to claim the use of 7-year data and all clinical studies, the MCM and LCM needed to show similar properties with the physical properties being used as a proxy for the clinical needs.[129]

Ultimately, Ethicon did not end up telling doctors that the mechanically cut mesh and the laser cut mesh are essentially the same, a decision that has kept doctors in the dark about the defects inherent in the mechanically cut TVT mesh, and has led to continued harms and hazards to women. In my opinion as a physician, Ethicon's decision to continue to market and sell the mechanically cut mesh, with all of its defects, and the decision to market the improved laser cut mesh as virtually the same as the old construction (Prolene) mesh, was clearly a decision by Ethicon to put profits before patient safety. In summary, for the reasons set forth

[127] Robinson Dep. (7/25/13) 585:12-23.
[128] *Id.*; ETH.MESH.00584291 (2/15/06 Email from Flatow, J.re DVer protocol for particle loss).
[129] ETH.MESH.00858252; *see also* ETH.MESH.00526473; ETH.MESH.02248778 (Kammerer PPT); Hellhammer Dep. (9/11/13) 120-121.

above, it is my opinion to a reasonable degree of medical certainty that the Prolene polypropylene mesh in the TVT has several characteristics that make it improper for use in the vaginal canal including particle loss, fraying, roping, curling, deformation and loss of pore size. These unwanted characteristics can lead to, among other things, an increased inflammatory response (particle loss and fraying) and/or increased pressure on the urethra (roping or curling) or loss of pore size (roping or curling), and can lead to a multitude of injuries, including such as multiple erosions that can occur throughout one's lifetime, chronic and debilitating pelvic pain, recurrence, worsening incontinence, chronic dyspareunia, wound infection, rejection of the mesh, sexual dysfunction, urinary and defecatory dysfunction, vaginal scarring, wound healing problems, injury to ureters, pelvic abscess formation, risk of infection, and/or the need for additional surgeries, among others. As a result, the polypropylene in Ethicon's TVT mesh (Prolene) is not suitable for its intended application as a permanent prosthetic implant for stress urinary incontinence in women.

Moreover, Ethicon did not inform physicians and patients that its mesh was susceptible to these physical deformations that could lead to painful erosions, recurrent, late infections and the need for mesh removal. Nor did Ethicon inform physicians that laser cut mesh had materially different mechanical properties than mechanically cut mesh. By failing to do so, Ethicon did not adequately warn physicians about these important risks, nor by extension, provide surgeons with an opportunity to discuss these risks with their patients.